



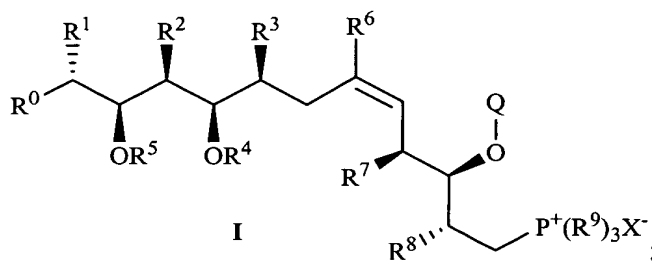
UPN-4377
Application No.: 10/817,532
Office Action Dated: March 6, 2006

PATENT

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Original) A process for preparing a compound of formula I:



wherein:

R^0 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $(CH_2)_r(C_{3-6}$ cycloalkyl), $(CH_2)_r$ (aryl) or $(CH_2)_r$ (heterocycle), wherein r is selected from 0, 1, 2, 3, and 4;

R^1 , R^2 , R^3 , R^6 , R^7 and R^8 are independently H or C_{1-10} alkyl;

R^4 is an acid labile hydroxyl protecting group;

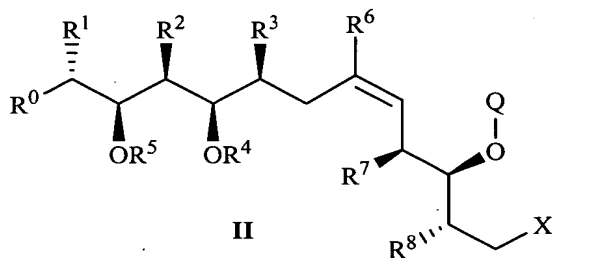
R^5 is an oxidatively labile hydroxyl protecting group;

each R^9 is independently C_{6-14} aryl;

Q is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and

X is halogen;

comprising contacting a compound of formula II:



wherein:

R^0 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $(CH_2)_r(C_{3-6}$ cycloalkyl), $(CH_2)_r$ (aryl) or $(CH_2)_r$ (heterocycle), wherein r is selected from 0, 1, 2, 3, and 4;

R^1 , R^2 , R^3 , R^6 , R^7 and R^8 are independently H or C_{1-10} alkyl;

R^4 is an acid labile hydroxyl protecting group;

R^5 is an oxidatively labile hydroxyl protecting group;

Q is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and

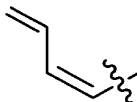
X is halogen;

at a pressure of less than about 10,000 psi with a phosphine of formula $P(R^9)_3$ wherein each R^9 is independently C_{6-14} aryl;

for a time and under conditions sufficient to prepare the compound of formula I.

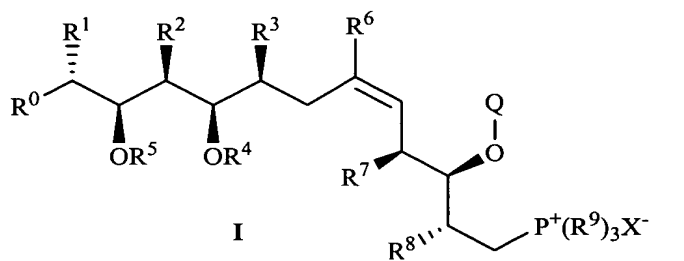
2. (Original) A process according to claim 1 wherein Q is methoxymethyl, methylthiomethyl, 2-methoxyethoxymethyl, acetyl, benzyloxymethyl, 2-(trimethylsilyl)ethoxymethyl or allyl.
3. (Original) A process according to claim 2 wherein Q is methoxymethyl.
4. (Original) A process according to claim 1 wherein the X moiety of the compound of formula II is iodo.
5. (Original) A process according to claim 1 further comprising a base.
6. (Original) A process according to claim 5 wherein the base is non-nucleophilic.
7. (Original) A process according to claim 6 wherein the base is isopropyl-diethylamine.
8. (Original) A process according to claim 1 wherein the reaction is carried out at essentially atmospheric pressure.
9. (Original) A process according to claim 1 wherein R^0 is alkenyl.

10. (Original) A process according to claim 9 wherein R⁰ is:



11. (Original) A process according to claim 1 wherein R¹, R², R³, R⁶, R⁷ and R⁸ are independently H or C₁₋₃ alkyl.
12. (Original) A process according to claim 1 wherein R¹, R², R⁷ and R⁸ are methyl and R³ and R⁶ are each independently H or methyl.
13. (Original) A process according to claim 1 wherein R¹, R², R³, R⁶, R⁷ and R⁸ are methyl.
14. (Original) A process according to claim 1 wherein R¹, R², R³, R⁷ and R⁸ are methyl and R⁶ is H.
15. (Original) A process according to claim 1 wherein the reaction temperature is in the range of about 0 to about 200°C.
16. (Original) A process according to claim 15 wherein the reaction temperature is in the range of about 20 to about 140°C.
17. (Original) A process according to claim 1 wherein the reaction pressure is in the range from about ambient to about 10,000 psi.
18. (Original) A process according to claim 17 wherein the reaction pressure is essentially ambient.
19. (Original) A process according to claim 1 wherein at least one of R⁹ is phenyl.
20. (Original) A process according to claim 1 wherein R⁵ is *para*-methoxybenzyl.

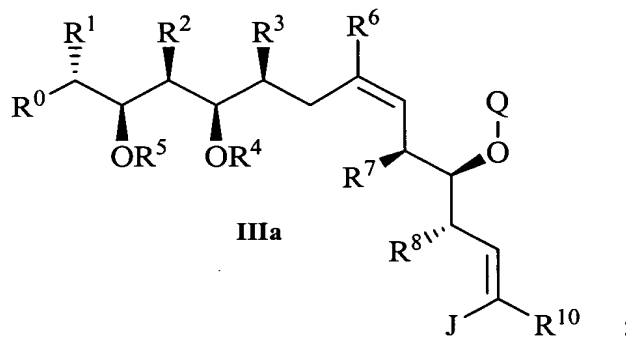
21. (Original) A process according to claim 1 wherein R^4 is $(R^{16})_3Si-$, and wherein each R^{16} is independently C_{1-6} alkyl.
22. (Original) A process according to claim 21 wherein R^4 is tert-butyldimethylsilyl.
23. (Original) A compound of the formula I:



wherein:

- R^0 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $(CH_2)_r(C_{3-6}$ cycloalkyl), $(CH_2)_r$ (aryl) or $(CH_2)_r$ (heterocycle), wherein r is selected from 0, 1, 2, 3, and 4;
- R^1 , R^2 , R^3 , R^6 , R^7 and R^8 are independently H or C_{1-10} alkyl;
- R^4 is an acid labile hydroxyl protecting group;
- R^5 is an oxidatively labile hydroxyl protecting group;
- each R^9 is independently C_{6-14} aryl;
- Q is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and
- X is halogen.

24. (Original) A process for preparing a compound of formula IIIa:



wherein:

R^0 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $(CH_2)_r(C_{3-6}$ cycloalkyl), $(CH_2)_r$ (aryl) or $(CH_2)_r$ (heterocycle), wherein r is selected from 0, 1, 2, 3, and 4;

R^1 , R^2 , R^3 , R^6 , R^7 and R^8 are independently H or C_{1-10} alkyl;

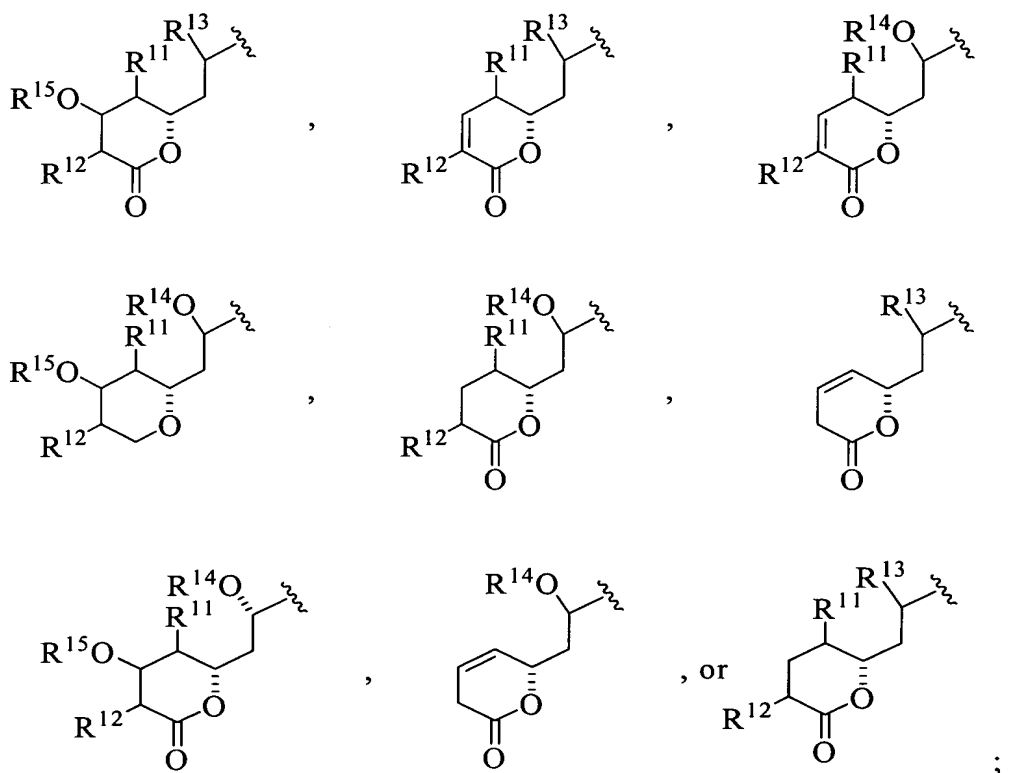
R^4 is an acid labile hydroxyl protecting group;

R^5 is an oxidatively labile hydroxyl protecting group;

R^{10} is H or C_1-C_6 alkyl;

Q is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom bonded to the oxygen of the hydroxyl group being protected; and

J is:

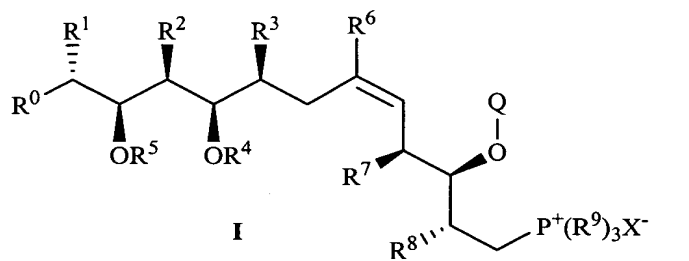


wherein:

R^{11} , R^{12} and R^{13} are each independently H or C_1-C_{10} alkyl; and

R^{14} and R^{15} are each independently H or an acid labile hydroxyl protecting group;

comprising contacting a compound of formula I:



wherein:

R^0 is C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $(CH_2)_r(C_{3-6}$ cycloalkyl), $(CH_2)_r(aryl)$ or $(CH_2)_r(heterocycle)$, wherein r is selected from 0, 1, 2, 3, and

4;

R^1, R^2, R^3, R^6, R^7 and R^8 are independently H or C_{1-10} alkyl;

R^4 is an acid labile hydroxyl protecting group;

R^5 is an oxidatively labile hydroxyl protecting group;

Q is H or an acid labile hydroxyl protecting group wherein the hydroxyl protecting group has a mass of 135 Daltons or less and is unbranched at the atom being protected;

each R^9 is independently C_{6-14} aryl; and

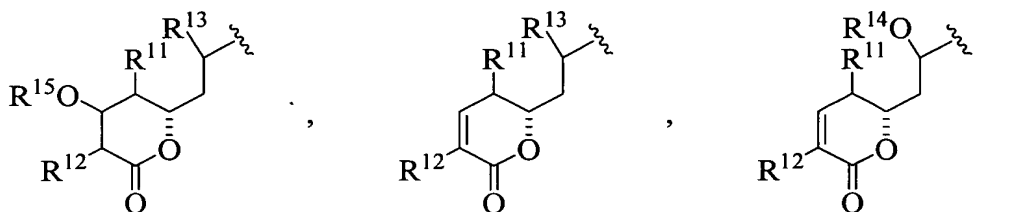
X is halogen;

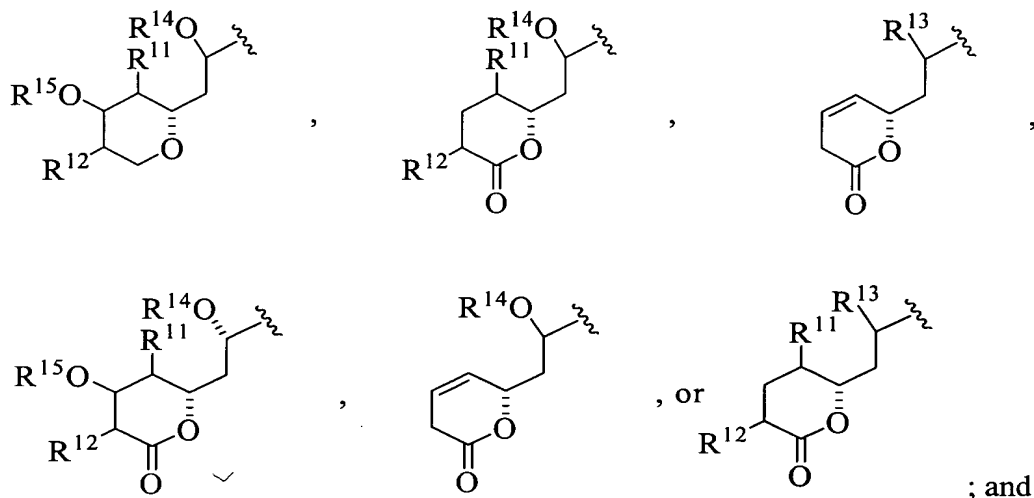
with a compound of formula $J-C(=O)R^{10}$,

wherein:

R^{10} is H or C_1-C_6 alkyl; and

J is:





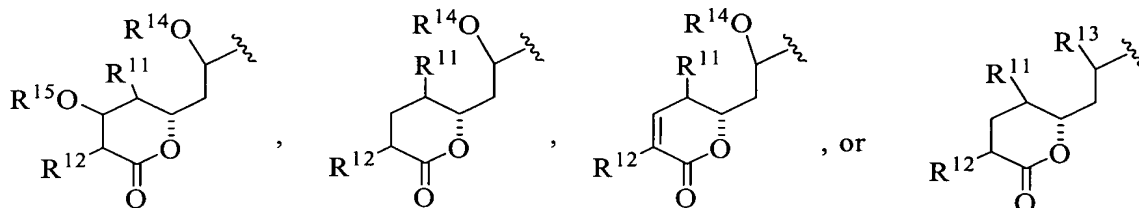
wherein:

R^{11} , R^{12} , R^{13} and R^{16} are each independently H or C_1 - C_{10} alkyl; and
 R^{14} and R^{15} are each independently H or an acid labile hydroxyl

protecting group;

in the presence of a base for a time and under conditions sufficient to prepare the compound of formula IIIa.

25. (Original) A process according to claim 24, wherein at least one of R^{14} and R^{15} is other than H.
26. (Original) A process according to claim 24, wherein the reaction is carried out at a temperature in the range of about -30 to about -78°C.
27. (Original) A process according to claim 24, wherein the reaction is carried out at a temperature of about -78°C.
28. (Original) A process according to claim 24, wherein R^{10} is H.
29. (Original) A process according to claim 24 wherein J is:

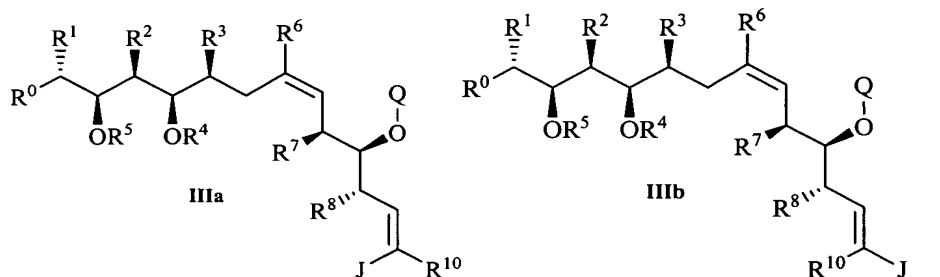


30. (Original) A process according to claim 24, wherein the base is NaHMDS, LiHMDS, KHMDS, MeLi-LiBr complex, n-BuLi (with or without HMPA), KOtBu or NaH.

31. (Original) A process according to claim 30, wherein the base is CH₃Li-CH₃Br complex.

32. (Original) A process according to claim 24, wherein the ratio of the compound of formula IIIa to a by-product compound of formula IIIb is at least about 4;

wherein the compounds of formula IIIa and IIIb have the structures:



33. (Original) A process according to claim 32, wherein the ratio of the compound of formula IIIa to the by-product compound of formula IIIb is at least about 10.